

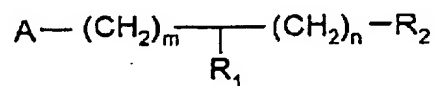
Amendments to the Claims

10/549942

JC17 Rec'd PCT/PTO 20 SEP 2005

Please amend the listing of claims as follows:

1. (Original) A compound of structural formula (I):



(I)

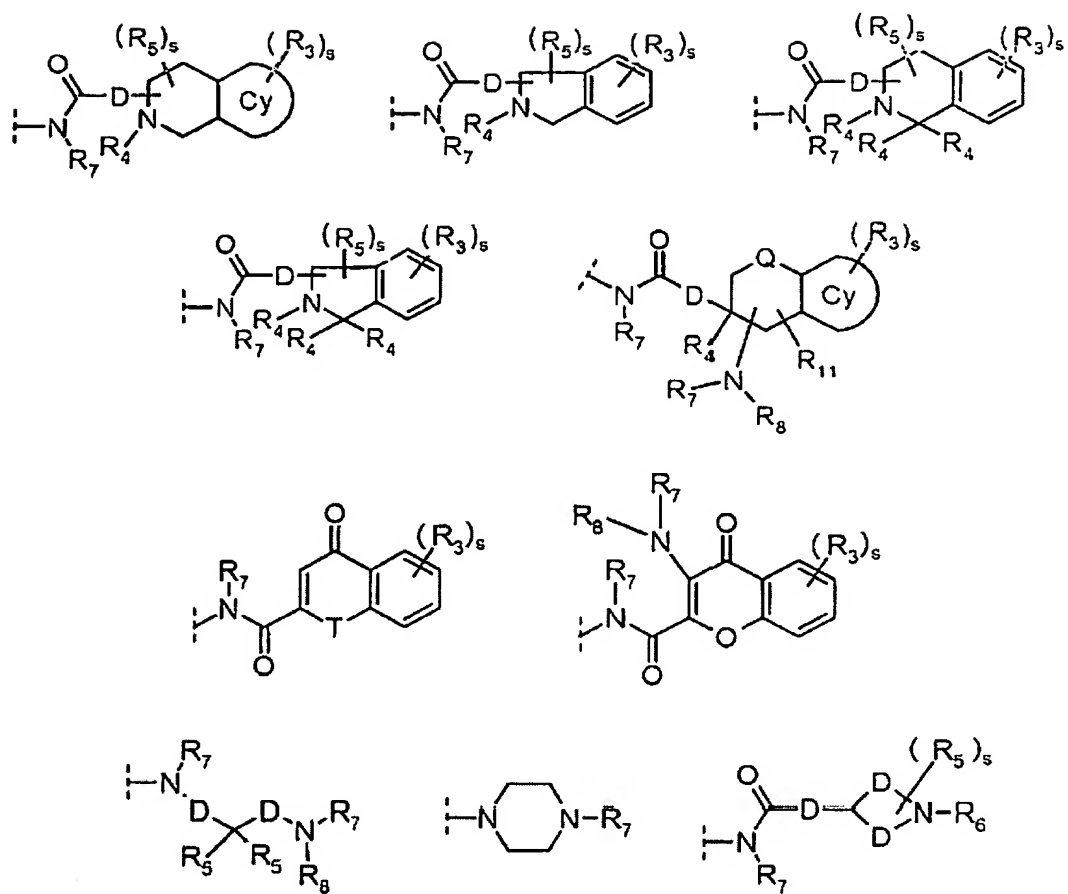
or a pharmaceutically acceptable salt or a solvate thereof, wherein

R₁ is:

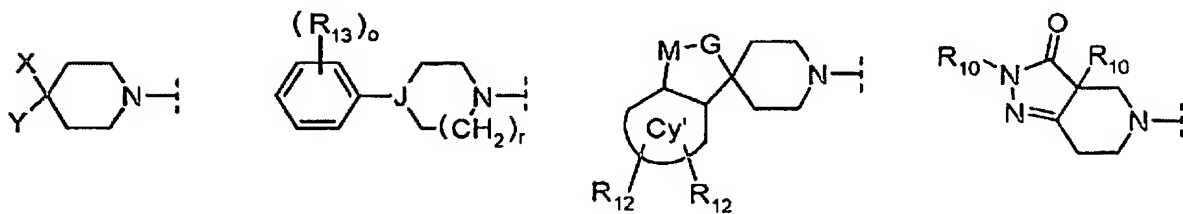
(D)-aryl or (D)-heteroaryl,

wherein aryl and heteroaryl are unsubstituted or substituted;

R_2 is:



A is:



each R₃ is independently:

hydrogen,
halo,
alkyl ,
haloalkyl,
hydroxy,
alkoxy,
S-alkyl,
SO₂-alkyl,
O-alkenyl,
S-alkenyl,
NR₁₅C(O)R₁₅,
NR₁₅SO₂R₁₅,
N(R₁₅)₂,
(D)-cycloalkyl,
(D)-aryl (wherein aryl is phenyl or naphthyl),
(D)-heteroaryl,
(D)-heterocyclyl (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and
wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted, and two adjacent R₃ may form a 4- to 7-membered ring;

each R₄ is independently:

hydrogen,
alkyl,
C(O)-alkyl,
SO₂alkyl,
SO₂aryl,
(D)-aryl or
(D)-cycloalkyl;

each R_5 is independently:

hydrogen,
alkyl,
(D)-aryl,
(D)-heteroaryl,
(D)- $N(R_7)_2$,
(D)- $NR_7C(O)$ -alkyl,
(D)- NR_7SO_2 -alkyl,
(D)- $SO_2N(R_7)_2$,
(D)- $(O)_q$ -alkyl,
(D)- $(O)_q(D)$ - NR_7COR_7 ,
(D)- $(O)_q(D)$ - $NR_7SO_2R_7$,
(D)- $(O)_q$ -heterocyclyl or
(D)- $(O)_q(alkyl)$ -heterocyclyl;

each R_6 is independently:

hydrogen,
alkyl,
(D)-phenyl,
 $C(O)$ -alkyl,
 $C(O)$ -phenyl,
 SO_2 -alkyl or
 SO_2 -phenyl;

R_7 and R_8 are each independently:

hydrogen,
alkyl or
(D)-cycloalkyl, or

R_7 and R_8 together with the nitrogen to which they are attached form a 5- to 8-membered ring optionally containing an additional heteroatom selected from O, S and NR₄,
wherein alkyl and cycloalkyl are unsubstituted or substituted;

R₁₀ is independently:

hydrogen,

alkyl,

(D)-aryl or

(D)-cycloalkyl;

R₁₁ is:

hydrogen or

alkyl;

R₁₂ is:

hydrogen,

halo,

alkyl,

alkoxy,

C≡N,

CF₃ or

OCF₃;

R₁₃ is independently:

hydrogen,

hydroxy,

cyano,

nitro,

halo,

alkyl,

alkoxy,

haloalkyl,

(D)-C(O)₁₅,

(D)-C(O)₁₅,

(D)-C(O)SR₁₅,

(D)-C(O)-heteroaryl,

(D)-C(O)-heterocyclyl,

(D)-C(O)N(R₁₅)₂,

$(D)-N(R_{15})_2$,
 $(D)-NR_{15}COR_{15}$,
 $(D)-NR_{15}CON(R_{15})_2$,
 $(D)-NR_{15}C(O)OR_{15}$,
 $(D)-NR_{15}C(R_{15})=N(R_{15})$,
 $(D)-NR_{15}C(=NR_{15})N(R_{15})_2$,
 $(D)-NR_{15}SO_2R_{15}$,
 $(D)-NR_{15}SO_2N(R_{15})_2$,
 $(D)-NR_{15}(D)\text{-heterocyclyl}$,
 $(D)-NR_{15}(D)\text{-heteroaryl}$,
 $(D)-OR_{15}$,
 OSO_2R_{15} ,
 $(D)-[O]_q(\text{cycloalkyl})$,
 $(D)-[O]_q(D)\text{-aryl}$,
 $(D)-[O]_q(D)\text{-heteroaryl}$,
 $(D)-[O]_q(D)\text{-heterocyclyl}$ (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen when $q=1$),
 $(D)-SR_{15}$,
 $(D)-SOR_{15}$,
 $(D)-SO_2R_{15}$ or
 $(D)-SO_2N(R_{15})_2$,
 wherein alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl and heteroaryl are unsubstituted or substituted;

each R_{15} is independently:

hydrogen,
 alkyl,
 haloalkyl,
 $(D)\text{-cycloalkyl}$,
 $(D)\text{-aryl}$ (wherein aryl is phenyl or naphthyl),
 $(D)\text{-heteroaryl}$,
 $(D)\text{-heterocyclyl}$ (wherein heterocyclyl excludes a heterocyclyl containing a single nitrogen), and

wherein aryl, heteroaryl, heterocyclyl, alkyl and cycloalkyl is unsubstituted or substituted;

R₁₇ is independently:

R₁₀ or
(D)-heterocyclyl;

R₁₈ is independently:

R₁₀,
(D)-heteroaryl,
(D)-heterocyclyl,
(D)-N(Y)₂,
(D)-NH-heteroaryl or
(D)-NH-heterocyclyl,

wherein aryl, heteroaryl, alkyl, D, cycloalkyl and heterocyclyl are unsubstituted or substituted, or

two R₁₈ groups together with the atoms to which they are attached form a 5- to 8-membered mono- or bi-cyclic ring system optionally containing an additional heteroatom selected from O, S, NR₁₀, NBoc and NZ;

Cy is:

aryl,
5- or 6-membered heteroaryl,
5- or 6-membered heterocyclyl or
5- or 7-membered carbocyclyl;

Cy' is:

benzene,
pyridine or
cyclohexane;

X is:

alkyl,
(D)-cycloalkyl,

(D)-aryl,
 (D)-heteroaryl,
 (D)-heterocyclyl,
 (D)-C \equiv N,
 (D)-CON(R₁₇R₁₇),
 (D)-CO₂R₁₇,
 (D)-COR₁₇,
 (D)-NR₁₇C(O)R₁₇,
 (D)-NR₁₇CO₂R₁₇,
 (D)-NR₁₇C(O)N(R₁₇)₂,
 (D)-NR₁₇SO₂R₁₇,
 (D)-S(O)_pR₁₇,
 (D)-SO₂N(R₁₇)(R₁₇),
 (D)-OR₁₇,
 (D)-OC(O)R₁₇,
 (D)-OC(O)OR₁₇,
 (D)-OC(O)N(R₁₇)₂,
 (D)-N(R₁₇)(R₁₇) or
 (D)-NR₁₇SO₂N(R₁₇)(R₁₇),

wherein aryl, heteroaryl, alkyl, D, cycloalkyl and heterocyclyl are unsubstituted or substituted;

Y is:

hydrogen,
 alkyl,
 (D)-cycloalkyl,
 (D)-aryl,
 (D)-heterocyclyl or
 (D)-heteroaryl,

wherein aryl, heteroaryl, alkyl, D and cycloalkyl are unsubstituted or substituted;

Q is a bond, O, S(O)_u, NR₆ or CH₂;

D is a bond or C₁ - C₄ alkyl;

E is O, S or NR₆;

G is D, CH-alkyl, O, C=O or SO₂, with the proviso that when G is O, the ring atom M is carbon;

J is N or CH;

M is CHCO₂Y, CHC(O)N(Y)₂, NSO₂R₁₈, CHN(Y)COR₁₈, CHN(Y)SO₂R₁₈, CHCH₂OY or CHCH₂heteroaryl;

T is O or NR₇;

n is 0 - 3;

m is 1 - 3;

o is 0 - 3;

p is 0 - 2;

q is 0 or 1;

r is 1 or 2;

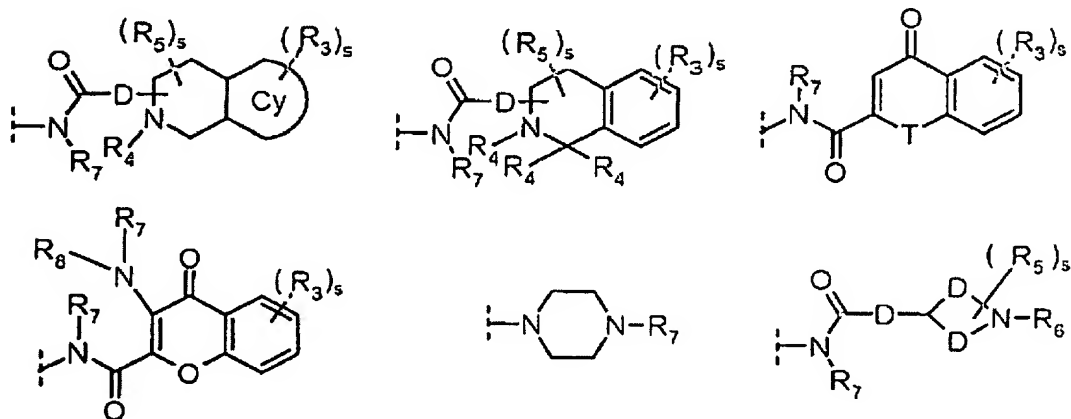
s is 0 - 3;

u is 0 - 2.

2. (Original) The compound of claim 1, wherein

R₁ is (D)-aryl which may be substituted with one to three substituents independently selected from the group consisting of cyano, nitro, perfluoroalkoxy, halo, alkyl (D)-cycloalkyl, alkoxy, hydroxy and haloalkyl;

R₂ is:



R₃ is independently:

hydrogen,
halo,
alkyl,
hydroxy,
alkoxy,
S-alkyl,
SO₂-alkyl,
O-alkenyl,
S-alkenyl,
haloalkyl or
(D)-cycloalkyl;

R₄ is:

hydrogen or
alkyl;

each R₅ is independently:

hydrogen,
alkyl,
(D)-aryl,
(D)-heteroaryl,
(D)-N(R₇)₂,
(D)-NR₇C(O)alkyl or
(D)-NR₇SO₂alkyl;

R₇ and R₈ are each independently:

hydrogen,
alkyl or
cycloalkyl, or

R₇ and R₈ together with the nitrogen to which they are attached form a 5- to 7-membered ring optionally containing an additional heteroatom selected from O, S and NR₄;

R₉ is:

alkyl,
OR₁₀,
(D)-aryl,
(D)-cycloalkyl,
(D)-heteroaryl and
halo;

R₁₂ is:

hydrogen,
halo,
alkyl,
alkoxy or
C \equiv N;

R₁₃ is independently:

hydrogen,
hydroxy,
cyano,
nitro,
halo,
alkyl,
alkoxy,
haloalkyl,
(D)-C(O)-heterocyclyl,
(D)-N(R₁₅)₂,
(D)-NR₁₅COR₁₅,
(D)-NR₁₅CON(R₁₅)₂,
(D)-NR₁₅C(O)OR₁₅,
(D)-NR₁₅C(R₁₅)=N(R₁₅),
(D)-NR₁₅C(=NR₁₅)N(R₁₅)₂,
(D)-NR₁₅SO₂R₁₅ or
(D)-NR₁₅SO₂N(R₁₅)₂;

each R₁₄ is independently:

hydrogen,
halo,
alkyl,
(D)-cycloalkyl,
alkoxy or
phenyl;

each R₁₅ is independently:

hydrogen,
halo,
alkyl,
(D)-cycloalkyl,
alkoxy or
phenyl;

each R₁₆ is independently:

hydrogen,
alkyl or
cycloalkyl;

X is:

alkyl,
(D)-cycloalkyl,
(D)-aryl,
(D)-heteroaryl,
(D)-heterocyclyl,
(D)-NHC(O)R₁₇,
(D)-CO₂R₁₇ or
(D)-CON(R₁₇R₁₇);

Y is:

hydrogen,
alkyl,

(D)-cycloalkyl,
(D)-aryl,
(D)-heterocyclyl or
(D)-heteroaryl;

Cy is:

aryl,
5- or 6-membered heteroaryl,
5- or 6-membered heterocyclyl or
5- to 7-membered carbocyclyl;

Cy' is benzene or pyridine;

D is a bond or C₁ - C₄-alkylene;

M is NSO₂R₁₈, CHN(Y)COR₁₈ or CHN(Y)SO₂R₁₈;

G is D or CH-alkyl;

T is NR₇ or O;

n is 0 or 1 ;

m is 1 or 2;

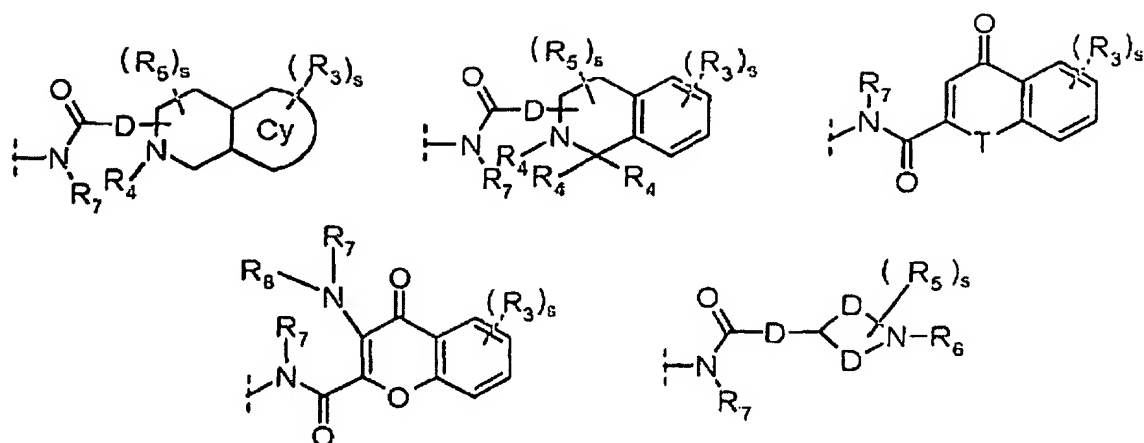
r is 1;

s is 0, 1 or 2.

3. (Currently Amended) The compound of ~~claims 1 or 2~~claim 1, wherein

R₁ is (D)-phenyl or (D)-naphthyl which may be substituted with one or two substituents independently selected from the group consisting of perfluoroalkoxy, halo, alkyl, alkoxy and haloalkyl;

R₂ is:



R₃ is hydrogen or halo;

R₄ is hydrogen;

R₅ is hydrogen;

R₇ and R₈ are each independently:

hydrogen or

alkyl, or

R₇ and R₈ together with the nitrogen to which they are attached form a 5- to 6-membered ring optionally containing an additional oxygen atom;

R₁₂ is:

hydrogen,

halo or

C₁ - C₄ alkyl;

R₁₃ is independently:

cyano,

nitro,

halo,

alkyl,
(D)-C(O)-heterocyclyl,
(D)-N(R₁₅)₂,
(D)-NR₁₅COR₁₅,
(D)-NR₁₅CON(R₁₅)₂,
(D)-NR₁₅C(O)OR₁₅ or
(D)-NR₁₅SO₂R₁₅;

each R₁₄ is independently:

hydrogen,
halo,
alkyl,
alkoxy or
phenyl;

each R₁₅ is independently:

hydrogen,
halo,
alkyl,
alkoxy or
phenyl;

X is:

alkyl,
(D)-cycloalkyl,
(D)-heterocyclyl,
(D)-NHC(O)R₁₇ or
(D)-CON(R₁₇R₁₇);

Y is:

hydrogen,
alkyl,
(D)-cycloalkyl or
(D)-heterocyclyl;

Cy is

aryl or

5- or 6-membered heteroaryl;

Cy' is benzene;

D is a bond or CH₂;

M is NSO₂R₁₈;

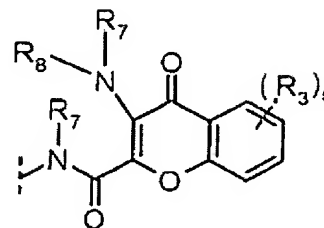
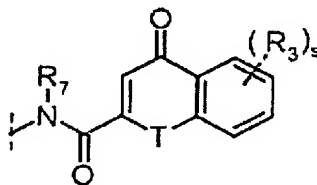
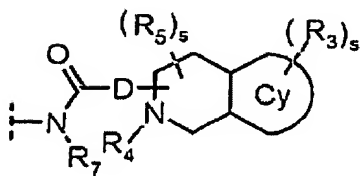
G is D;

s is 0 or 1 .

4. (Currently Amended) The compound of ~~any of claims 1 to 3~~ claim 1, wherein

R₁ is (CH₂)-phenyl or (CH₂)-naphthyl which may be substituted with one to three halo atoms;

R₂ is:



R₁₂ is hydrogen;

R₁₃ is independently:

cyano,

nitro,

halo or

(D)-NR₁₅COR₁₅;

X is:

C₁ - C₄ alkyl,

C₅ - C₇ cycloalkyl,

(D)-CON(R₁₇R₁₇) or
N-containing heterocyclyl;

Y is:

hydrogen,
C₁ - C₄ alkyl or
C₅ - C₇ cycloalkyl;

Cy is aryl;

G is CH₂.

5. (Currently Amended) ~~The compound of any of claims 1 to 4 for use as a~~
A medicament comprising the compound of claim 1.

6. (Currently Amended) ~~Use of the compound of any of claims 1 to 4 for the~~
~~preparation of a medicament for the treatment or prevention of~~ A method of treating or
preventing disorders, diseases or conditions responsive to the modulation of the
melanocortin-4 receptor in a mammal, where modulation means activation in the case of
MC4-R agonists or inactivation in the case of MC4-R antagonists, the method comprising
administering to a human or mammal an effective amount of the compound of claim 1.

7. (Currently Amended) ~~Use of MC4-R antagonists according to claims 6 for the~~
~~preparation of a medicament for the treatment or prevention of cancer cachexia.~~ A method of
treating or preventing cancer cachexia, the method comprising administering to a human or
mammal an effective amount of the MC4-R antagonists according to claim 6.

8. (Currently Amended) ~~Use of MC4-R antagonists according to claims 6 for the~~
~~preparation of a medicament for the treatment or prevention of muscle wasting.~~ A method of
treating or preventing muscle wasting, the method comprising administering to a human or
mammal an effective amount of the MC4-R antagonists according to claim 6.

9. ~~(Currently Amended) Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of anorexia.~~ A method of treating or preventing anorexia, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

10. ~~(Currently Amended) Use of MC4-R antagonists according to claims 6 for the preparation of a medicament for the treatment or prevention of anxiety and/or depression.~~ A method of treating or preventing anxiety and/or depression, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

11. ~~(Currently Amended) Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of obesity.~~ A method of treating or preventing obesity, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

12. ~~(Currently Amended) Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of diabetes mellitus.~~ A method of treating or preventing diabetes mellitus, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

13. ~~(Currently Amended) Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of male or female sexual dysfunction.~~ A method of treating or preventing male or female sexual dysfunction, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

14. ~~(Currently Amended) Use of MC4-R agonists according to claims 6 for the preparation of a medicament for the treatment or prevention of erectile dysfunction.~~ A method of treating or preventing erectile dysfunction, the method comprising administering to a human or mammal an effective amount of the MC4-R antagonists according to claim 6.

15. (Currently Amended) A pharmaceutical composition which comprises a compound ~~of any of claims 1 to 4~~claim 1 and a pharmaceutically acceptable carrier.